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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,983	10/31/2003	Howard Sands	12636.304.201	8849

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EXAMINER	
LANDAU, SHARMILA GOLLAMUDI	
ART UNIT	**PAPER NUMBER**
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/698,983	SANDS ET AL.	
	Examiner	Art Unit	
	Sharmila Gollamudi Landau	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43 and 49-70* is/are pending in the application.

4a) Of the above claim(s) *8,9 and 49-70* is/are withdrawn from consideration.

5)☐ Claim(s) ____ is/are allowed.

6)☒ Claim(s) *1-7 and 10-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Applicant's Amendments and Response to Election Restriction Requirement filed 4/18/07 are acknowledged.

Election/Restrictions

Applicant's election without traverse of Group I claims 1-43 and 49-70 and species: cytidine analog, in the reply filed on 4/18/07 is acknowledged. Accordingly, claims 1-7, 10-43 are pending as being directed to the elected invention and species. Claims 8-9 and 49-70 are withdrawn as being directed to the non-elected invention and specie.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-18, 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 15-18 and 29 contains the trademark/trade name EUDRAGIT; EUDRAGIT L100; EUDRAGIT L100-55; and TWEEN 80 respectively. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or

trade name. In the present case, the trademark/trade name is used to identify/describe a enteric polymer (EUDRAGIT) and surfactant (TWEEN 80) respectively and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 10-12, 15-17, 19-20, 23-28, 30-33, 35-37, 40-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Bergstrand et al (5,817,338).

Bergstrand et al disclose a tableted dosage form comprising omeprazole or a salt thereof. See abstract. Bergstrand discloses omeprazole is susceptible to degradation/transformation in acidic and neutral media (acid labile). See column 1, lines 45-51. The examples utilize omeprazole, sodium omeprazole, and magnesium omeprazole. Omeprazole is water-soluble (0.5mg/ml), albeit poorly water-soluble and independent claim 1 does not define the water-solubility of the drug. With regard to claims 2-3, magnesium omeprazole is water-soluble and has a solubility of 0.25g/l.

Example 1 discloses a tablet comprising a 1) core containing magnesium omeprazole, mannitol, microcrystalline cellulose, hydroxypropyl cellulose, and sodium lauryl sulfate; 2) a separating layer comprising hydroxypropylmethylcellulose; 3) an enteric coating comprising methacrylic acid copolymer (note that eudragit polymers are methacylic acid copolymers; also note the 112, 2nd paragraph rejection). Other enteric coating polymers disclosed include cellulose

acetate phthalate(dissolves at a pH of 6), hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, polyvinyl acetate phthalate (dissolves at a pH of 5), cellulose acetate trimellitate, carboxymethylethylcellulose, and shellac (dissolves at a pH of 7). See column 5, lines 45-56. Example 2 discloses a enteric coating composition comprising Polysorbate 80 and triethyl citrate. The tablet of example 1 has a hardness of 110-120N (11.21-12.23 kp). The tablets comprise 1-400mg of the active. Example 2 discloses 10mg. A pH buffering salt is disclosed on column 6, lines 20-40. Example 10 utilizes sodium phosphate. Example 12 utilizes magnesium stearate and talc.

Claims 1, 4-5, 10-12, 15, 19-20, 23, 25-26, 30-34, 36-38, 40-43 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Darder et al (20020098242).

Darder discloses a pharmaceutical composition comprising an acid-labile compound including omeprazole, lansoprazole, etc. coated with an enteric coating. Omeprazole is water-soluble, albeit poorly water-soluble; however independent claim 1 does not define the water-solubility of the drug. Lansoprazole has a water-solubility of 0.97 mg/l. Darder discloses combining the drug, a binder, a buffer, a surfactant, a filling material (lactose, starch, saccharose, mannitol, sorbitol, gelatin or microcrystalline cellulose), and a disintegrating-swelling compound (starch, calcium carboxymethyl cellulose, sodium glycolate starch or hydroxypropyl cellulose). The enteric coating comprises plasticizers, surfactants, lubricants (magnesium stearate, talc) and an enteric coating polymer (polyacrylic acids, methacrylics and their salts, HPMC acetate succinate, polyvinyl acetate phthalate). See [0051]-[0062].

Example 1 discloses a pellet comprising lansoprazole, sodium lauryl sulfate, disodium phosphate, lactose, hydroxypropylmethylcellulose, and hydroxypropylcellulose. The pellet is

coated with an enteric coating comprising talc, titanium dioxide, PEG 6000, polysorbate, and Eudragit L30D55.

Claims 1, 4-5, 10-12, 15-17, 19-20, 25-28, 30, 32-33, 35, 40, 41 are rejected under 35 U.S.C. 102 (e) as being anticipated by Patel et al (20030180352).

Patel discloses solid carriers for improved delivery of active ingredients in pharmaceutical compositions. See abstract. Patel discloses various actives may be utilized including acid labile drugs, which degrade quickly when in contact with acid. Patel discloses an enteric coating therefore is typically applied to a core containing such acid-labile drugs was applied to prevent the drug from contacting the acidic pH conditions of the stomach upon oral administration. The acidic residue of the enteric coating, however, can degrade the acid-labile drug during storage. To solve this problem, a significant amount of inorganic alkaline materials were introduced to the core by specific processes, such as granulation so as to ensure the acid-labile drug being evenly in contact with the basic inorganic salt. [0008]. A preferred class of acid-labile active ingredients are benzimidazoles, particularly those useful as proton pump inhibitors such as esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole, and pharmaceutically acceptable salts. Exemplary salts include the sodium, potassium, calcium and magnesium salts of the active ingredient. [0115].

The preferred enteric coating polymers disclosed include shellac (dissolves in a media of 7 and greater); Eudragit L, L-30D which is insoluble in a pH of less than 5.5, and S which are insoluble at a pH of 5.5 and below and soluble at a pH of 7 and above; PVAP which dissolves in a pH of 5. The coating solution comprises talc and/or magnesium stearate; plasticizers including triethyl citrate and triacetin; and colorants. [0289-0302]. Eudragit L 100-55 is disclosed. [0034].

Example 5 comprises a bead containing omeprazole, PEG1-50 monostearate, PEG-40 monostearate, and magnesium carbonate (buffer salt). The bead is coated with a protective polymer layer (reads on seal coat) comprising hydroxypropylmethylcellulose (retention enhancing agent), talc, and triethylcitrate. The bead if then further coated with an enteric coating of Eudragit L100, triethyl citrate, and talc. Example 7-8. Example 29-34 disclose 0.5% lansoprazole beads coated with a seal coat and an enteric coating. Example 32 discloses lansoprazole and PEG 4600 (retention enhancing excipient). Omeprazole is water-soluble, albeit poorly water-soluble; however independent claim 1 does not define the water-solubility of the drug. Lansoprazole has a water-solubility of 0.97 mg/l.

Claims 1-6, 10-12, 15, 19-20, 23, 26, 32-34, 36-39, 42-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Wechter et al (3,920,630).

Wechter discloses a tablet composition comprising 2,2-anhydro-ara-cytidine. The oral dosage form comprises a diluent and carrier including cornstarch, lactose, talc, stearic acid, gums, and magnesium stearate. See column 6, lines 45-67. Example 7 discloses a tablet comprising 2,2-anhydro-ara-cytidine hydrochloride, lactose, and talc. The tablet is coated with an enteric coating comprising cellulose acetate phthalate (dissolves at a pH of 6).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-3, 6-7, 13-14, 18, 21-23, 29, 36-39, 42-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patel et al (20030180352).

The teachings of Patel have been set forth above. Patel teaches the terms "active agent," "pharmacologically active agent," and "drug" are used interchangeably herein to refer to any chemical compound, complex or composition that has a beneficial biological effect, preferably a therapeutic effect in the treatment of a disease or abnormal physiological condition. [0051]. The active can include anti-cancer agents including decitabine. [0076]. Patel teaches the use of various excipients including surfactants such as polysorbate 80 (TWEEN 80); anti-adherents such as magnesium stearate, stearic acid, silica, starch; binders including methylcelloluse in an amount of 0.1-5%; diluents including talc, lactose, mannitol, microcrystalline cellulose, sodium starch glycolate; plasticizers including triacetin and triethyl citrate. See [0252], [0241], [0237], [0201]. The coating comprises plasticizers such as triacetin or triethyl citrate, colorants, talc, and/or magnesium stearate. Patel teaches the coating thickness must be sufficient to ensure that the oral dosage form remains intact until the desired site of topical delivery in the lower intestinal tract is reached. [0302]. Patel teaches Eudragit S is insoluble at pH below 5.5, but unlike Eudragit L-30-D, is poorly soluble in gastrointestinal fluids having pH of 5.5-7.0, such as is present in the small intestine media. This copolymer is soluble at pH 7.0 and above, i.e., the pH generally found in the colon. Eudragit S can be used alone as a coating to provide delivery of beginning at the large intestine via a delayed release mechanism. In addition, Eudragit S, being poorly soluble in intestinal fluids below pH 7, can be used in combination with Eudragit L-30-D, soluble in intestinal fluids above pH 5.5, in order to effect a delayed release composition. The more Eudragit L-30 D used, the more proximal release and delivery begins, and the more

Eudragit S used, the more distal release and delivery begins. [0305]. Patel teaches "extended release coating" designed to effect delivery over an extended period of time. Preferably, the extended release coating is a pH-independent coating formed of, for example, ethyl cellulose, hydroxypropyl cellulose, methylcellulose, hydroxymethyl cellulose, hydroxyethyl cellulose, acrylic esters, or sodium carboxymethyl cellulose. Patel teaches various extended release dosage forms can be readily designed by one skilled in art to achieve delivery to both the small and large intestines, to only the small intestine, or to only the large intestine, depending upon the choice of coating materials and/or coating thickness. [0279]. Suitable dosage forms include tablets. [0272].

Although Patel discloses decitabine, one cannot immediately envisage the use of decitabine in the dosage form. Further, the disintegration of the enteric coating and amount of enteric coating in term of weight percent are not specified.

However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to look to the guidance provided by Patel and utilize decitabine as the active of choice. One would have been motivated to do so with a reasonable expectation of success since Patel teaches decitabine is a suitable anti-cancer agent to utilize. Thus, if one desired to formulate a composition to treat cancer, a skilled artisan would have been motivated to select decitabine.

With regard to claims 13-14, 21-22, Patel teaches the amount of the enteric coating used and the type of enteric coating polymer or combinations of the enteric coating polymers provide the desired release in the given area of the intestine and within the given time frame. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made

to manipulate the amount of the enteric coating utilized and the types of polymers used to provide the desired targeted release.

With regard to claim 18 and 29, Patel teaches the enteric coating comprises plasticizers including triacetin and triethyl citrate. Triethyl citrate is exemplified. It would have been obvious for a skilled artisan to utilize either plasticizer taught by Patel since both are taught to be suitable plasticizers. Further, Patel teaches the enteric coating may comprise known excipients. Patel teaches polysorbate 80. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further utilize a known surfactant in the enteric coating composition.

Conclusion

All the claims are rejected at this point.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila Gollamudi Landau whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharmila Gollamudi Landau
Primary Examiner
Art Unit 1616

SGL